KAL
01-03-01

```
=> b medline lifesci embase biosis

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'MEDLINE' ENTERED AT 17:08:14 ON 02 JAN 2002

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FILE 'BIOSIS' ENTERED AT 17:08:14 ON 02 JAN 2002
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=> e koziel ?/au

E1            1     KOZIEK F/AU
E2            1     KOZIEKO T A/AU
E3            0 --> KOZIEL ?/AU
E4            1     KOZIEL B/AU
E5            3     KOZIEL C/AU
E6            1     KOZIEL CAROLYN/AU
E7           18     KOZIEL E/AU
E8            2     KOZIEL EDYTA/AU
E9            1     KOZIEL EWA/AU
E10          84     KOZIEL H/AU
E11           1     KOZIEL H A/AU
E12          22     KOZIEL HENRY/AU

=> s e4-12

L1          133 ("KOZIEL B"/AU OR "KOZIEL C"/AU OR "KOZIEL CAROLYN"/AU OR
"KOZIE
                L E"/AU OR "KOZIEL EDYTA"/AU OR "KOZIEL EWA"/AU OR "KOZIEL
H"/AU
                 OR "KOZIEL H A"/AU OR "KOZIEL HENRY"/AU)

=> s l1 and pepc

L2            0 L1 AND PEPC

=> e koziel h?/au

E1           84     KOZIEL H/AU
E2            1     KOZIEL H A/AU
E3            0 --> KOZIEL H?/AU
E4           22     KOZIEL HENRY/AU
E5            6     KOZIEL J/AU
E6           11     KOZIEL J A/AU
E7            1     KOZIEL JACEK/AU
E8            1     KOZIEL JACEK A/AU
E9            1     KOZIEL K/AU
E10          36     KOZIEL M/AU
E11          44     KOZIEL M G/AU
E12          57     KOZIEL M J/AU
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=> s koziel/au

L3            0 KOZIEL/AU

=> s e1-12

L4          262 ("KOZIEL H"/AU OR "KOZIEL H A"/AU OR "KOZIEL H?"/AU OR "KOZIEL
                HENRY"/AU OR "KOZIEL J"/AU OR "KOZIEL J A"/AU OR "KOZIEL
JACEK"/
                AU OR "KOZIEL JACEK A"/AU OR "KOZIEL K"/AU OR "KOZIEL M"/AU OR
                "KOZIEL M G"/AU OR "KOZIEL M J"/AU)

=> e koziel m?/au

E1            44      KOZIEL M G/AU
E2            57      KOZIEL M J/AU
E3             0 --> KOZIEL M?/AU
E4             4      KOZIEL MARGARET/AU
E5            10      KOZIEL MARGARET J/AU
E6             1      KOZIEL MARGARET JAME/AU
E7             8      KOZIEL MARGARET JAMES/AU
E8             1      KOZIEL MICHAEL/AU
E9            19      KOZIEL MICHAEL G/AU
E10            1      KOZIEL MICHAEL GENE/AU
E11            2      KOZIEL MIKE/AU
E12            1      KOZIEL N/AU

=> s e1-12

L5          184 ("KOZIEL M G"/AU OR "KOZIEL M J"/AU OR "KOZIEL M?"/AU OR
"KOZIEL
                 MARGARET"/AU OR "KOZIEL MARGARET J"/AU OR "KOZIEL MARGARET
                JAME"/AU OR "KOZIEL MARGARET JAMES"/AU OR "KOZIEL MICHAEL"/AU
                OR "KOZIEL MICHAEL G"/AU OR "KOZIEL MICHAEL GENE"/AU OR
"KOZIEL
                MIKE"/AU OR "KOZIEL N"/AU)

=> d history


     (FILE 'HOME' ENTERED AT 17:07:59 ON 02 JAN 2002)

     FILE 'MEDLINE, LIFESCI, EMBASE, BIOSIS' ENTERED AT 17:08:14 ON 02 JAN
2002
                 E KOZIEL ?/AU
L1            133 S E4-12
L2              0 S L1 AND PEPC
                 E KOZIEL H?/AU
L3              0 S KOZIEL/AU
L4            262 S E1-12
                 E KOZIEL M?/AU
L5            184 S E1-12

=> s l1 or l4 or l5

L6          335 L1 OR L4 OR L5

=> s l6 and pepc

L7            0 L6 AND PEPC

=> e koziel n?/au

E1            2      KOZIEL MIKE/AU
E2            1      KOZIEL N/AU
E3            0 --> KOZIEL N?/AU
```

```
E4            1     KOZIEL R G/AU
E5           12     KOZIEL S/AU
E6            3     KOZIEL S M/AU
E7            1     KOZIEL SCHMINDA E/AU
E8            6     KOZIEL SLAWOMIR/AU
E9            1     KOZIEL SLAWOMIR MAREK/AU
E10          81     KOZIEL V/AU
E11           1     KOZIEL VIGNERON RECHENMANN V R V/AU
E12           1     KOZIEL VIGNERON V/AU

=> s e1-12

L8          110 ("KOZIEL MIKE"/AU OR "KOZIEL N"/AU OR "KOZIEL N?"/AU OR
"KOZIEL
                R G"/AU OR "KOZIEL S"/AU OR "KOZIEL S M"/AU OR "KOZIEL
SCHMINDA
                E"/AU OR "KOZIEL SLAWOMIR"/AU OR "KOZIEL SLAWOMIR MAREK"/AU OR
                "KOZIEL V"/AU OR "KOZIEL VIGNERON RECHENMANN V R V"/AU OR
"KOZIE
                L VIGNERON V"/AU)

=> s l6 or l8

L9          442 L6 OR L8

=> e koziel vi?/au

E1            1     KOZIEL SLAWOMIR MAREK/AU
E2           81     KOZIEL V/AU
E3            0 --> KOZIEL VI?/AU
E4            1     KOZIEL VIGNERON RECHENMANN V R V/AU
E5            1     KOZIEL VIGNERON V/AU
E6           28     KOZIEL VIOLETTE/AU
E7            2     KOZIELEC G/AU
E8            1     KOZIELEC G E/AU
E9            6     KOZIELEC G F/AU
E10           1     KOZIELEC GREGORY/AU
E11           2     KOZIELEC GREGORY F/AU
E12           9     KOZIELEC J/AU

=> s e6

L10          28 "KOZIEL VIOLETTE"/AU

=> d history


     (FILE 'HOME' ENTERED AT 17:07:59 ON 02 JAN 2002)

     FILE 'MEDLINE, LIFESCI, EMBASE, BIOSIS' ENTERED AT 17:08:14 ON 02 JAN
2002
                E KOZIEL ?/AU
L1           133 S E4-12
L2             0 S L1 AND PEPC
                E KOZIEL H?/AU
L3             0 S KOZIEL/AU
L4           262 S E1-12
                E KOZIEL M?/AU
L5           184 S E1-12
L6           335 S L1 OR L4 OR L5
L7             0 S L6 AND PEPC
                E KOZIEL N?/AU
L8           110 S E1-12
L9           442 S L6 OR L8
                E KOZIEL VI?/AU
L10           28 S E6
```

=>

=> s l10 or l9

L11 470 L10 OR L9

=> s l11 and pollen

L12 1 L11 AND POLLEN

=> d l12

L12 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOSIS
AN 1996:15234 BIOSIS
DN PREV199698587369
TI Biolistic introduction of a synthetic Bt gene into elite maize.
AU Hill, M.; Launis, K.; Bowman, C.; McPherson, K.; Dawson, J.; Watkins, J.; **Koziel, M.**; Wright, M. S.
CS Ciba Biotechenol., P.O. Box 12257, Research Triangle Park, NC 27709-2257 USA
SO Euphytica, (1995) Vol. 85, No. 1-3, pp. 119-123.
ISSN: 0014-2336.
DT Article
LA English

=> s l11 and pepc

L13 0 L11 AND PEPC

=> s l11 and promoter

L14 16 L11 AND PROMOTER

=> dup rem l14

PROCESSING COMPLETED FOR L14
L15 8 DUP REM L14 (8 DUPLICATES REMOVED)

=> d l15 ibib abs tot

L15 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2000:334977 BIOSIS
DOCUMENT NUMBER: PREV200000334977
TITLE: Nucleic acid **promoter** fragment isolated from a plant tryptophan synthase alpha subunit (trpA) gene.
AUTHOR(S): **Koziel, Michael G. (1)**; Desai, Nalini M.; Lewis, Kelly S.; Kramer, Vance C.; Warren, Gregory W.; Evola, Stephen V.; Wright, Martha S.; Launis, Karen L.; Rothstein, Steven J.; Bowman, Cindy G.; Dawson, John L.; Dunder, Erik M.; Pace, Gary M.; Suttie, Janet L.
CORPORATE SOURCE: (1) Cary, NC USA
ASSIGNEE: Novartis Finance Corporation
PATENT INFORMATION: US 6018104 January 25, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 25, 2000) Vol. 1230, No. 4, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB DNA sequences optimized for expression in plants are disclosed. The DNA sequences preferably encode for an insecticidal polypeptides, particularly

insecticidal proteins from Bacillus thuringiensis. Plant promoters, particular tissue-specific and tissue-preferred promoters are also provided. Additionally disclosed are transformation vectors comprising said DNA sequences. The transformation vectors demonstrate high levels of insecticidal activity when transformed into maize.

L15 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1999:96778 BIOSIS
DOCUMENT NUMBER: PREV199900096778
TITLE: Synthetic DNA sequences having enhanced activity in maize.
AUTHOR(S): **Koziel, M. G.**; Desai, N. M.; Lewis, K. S.; Warren, G. W.; Evola, S. V; Crossland, L. D.; Wright, M. S.; Merlin, E. J.; Launis, K. L.; Bowman, C. G.; Dawson, J. L.; Dunder, E. M.; Pace, G. M.; Suttie, J. L.
CORPORATE SOURCE: Cary, N.C. USA
ASSIGNEE: NOVARTIS CORPORATION
PATENT INFORMATION: US 5859336 Jan. 12, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 12, 1999) Vol. 1218, No. 2, pp. 1439.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L15 ANSWER 3 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 97250930 MEDLINE
DOCUMENT NUMBER: 97250930 PubMed ID: 9096613
TITLE: Transgenic expression of hepatitis C virus structural proteins in the mouse.
AUTHOR: Kawamura T; Furusaka A; **Koziel M J**; Chung R T; Wang T C; Schmidt E V; Liang T J
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Charlestown, MA 02129, USA.
CONTRACT NUMBER: CA 54524 (NCI)
DK01952 (NIDDK)
RO1-CA63117 (NCI)
+
SOURCE: HEPATOLOGY, (1997 Apr) 25 (4) 1014-21.
Journal code: GBZ; 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970501

AB Although hepatitis C virus (HCV) is a leading cause of morbidity and mortality worldwide, the role of viral cytopathic effects remains unclear.

To study the biosynthesis of HCV structural proteins and their pathogenic role, we constructed transgenic mice, expressing type 1b HCV structural proteins (core, E1, and E2) in liver tissues. Two liver-specific promoters were used. The mouse major urinary protein (MUP) **promoter** has been shown to be developmentally regulated with little or no expression in utero but high-level expression after birth. The albumin (Alb) **promoter** provides constitutive, high levels of transgenes in live. Expression of both HCV transgenes was detected in several lines by Northern blots, HCV-specific reverse transcriptase-polymerase chain reactions (RT-PCR), and Western immunoblotting. Alb HCV lines showed higher levels of HCV expression than the MUP HCV lines.

Immunohistochemical analysis revealed a predominantly cytoplasmic presence

of core protein with occasional nuclear staining, and both cytoplasmic and membrane expression of the E2 protein in the transgenic livers. In both transgenes, the highest levels of both antigens were seen in perivenular hepatocytes, suggesting potential processing specificity in those cells. At six months of age, the livers of all transgenic lineages remained histologically normal. We concluded that HCV structural proteins are not directly cytopathic in this animal model.

L15 ANSWER 4 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96246645 EMBASE
DOCUMENT NUMBER: 1996246645
TITLE: Transgenic maize for the control of European corn borer and other maize insect pests.
AUTHOR: **Koziel M.G.**; Carozzi N.B.; Desai N.; Warren G.W.; Dawson J.; Dunder E.; Launis K.; Evola S.V.
CORPORATE SOURCE: Ciba Agr. Biotechnol. Research Unit,Research Triangle Park, NC 27709, United States
SOURCE: Annals of the New York Academy of Sciences, (1996) 792/- (164-171).
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Our results demonstrate that maize plants are protected from severe European corn borer infestations by expression of a synthetic gene encoding the active portion of the CryIA(b) .delta.-endotoxin from Bt. Different promoters, including three different tissue-specific promoters from maize, have proven effective in expressing insecticidal levels of CryIA(b) in tissues eaten by ECB. Use of transgenic crops to limit insect damage is a new technology. They provide new alternatives to be used with other options already available to protect crops. Plants producing a .delta.-endotoxin from Bt, like those derived from event 176, are the first to be commercialized as insect-tolerant transgenic crops, offering growers a new source of protection from damage caused by insect pests. As additional sources of insecticidal proteins or compounds are identified and characterized, new alternatives will also become available. These new alternatives will allow the control of insect pests not susceptible to known Bt .delta.-endotoxins and will further assist the management of resistance to the new traits and chemical insecticides if such resistance should arise. Agricultural biotechnology is in its infancy, and the available technology continues to improve at a rapid pace. More crops can be transformed now, and factors that control gene expression are becoming better understood. As this technology improves and the number of known insecticidal proteins and compounds increases, options for insect control will also increase. Likewise, as crops are transformed with new resistance traits, these traits will become part of the gene pool of that species and will be available for wider use in many varieties produced through traditional plant breeding. Transgenes will soon become part of the genetic diversity of many crops providing important pest control options.

L15 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1996:15234 BIOSIS
DOCUMENT NUMBER: PREV199698587369
TITLE: Biolistic introduction of a synthetic Bt gene into elite maize.
AUTHOR(S): Hill, M.; Launis, K.; Bowman, C.; McPherson, K.; Dawson, J.; Watkins, J.; **Koziel, M.**; Wright, M. S.
CORPORATE SOURCE: Ciba Biotechenol., P.O. Box 12257, Research Triangle Park,

NC 27709-2257 USA
SOURCE: Euphytica, (1995) Vol. 85, No. 1-3, pp. 119-123.
ISSN: 0014-2336.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A synthetic Bt gene encoding a truncated version of the CryIA(b) protein derived from Bacillus thuringiensis was successfully introduced into elite maize using microprojectile bombardment of immature embryos. The method used to initiate and identify transformation events is described. We describe the detailed parameters used for the Biolistics device as well as the plasmids used for the transformations. The plasmids contained the synthetic Bt gene driven by either the 35S CaMV **promoter** or a combination of two tissue-specific promoters, leaf and pollen, derived from maize. Specific conditions for the culture of Type I callus from immature embryos, the phosphinothricin (PPT) selection protocol, and the regeneration of plants are discussed. T0 and T1 plants were initially identified using the pH-dependent chlorophenol red test and/or the histochemical beta-glucuronidase (GUS) assay. PCR and Southern data confirm the presence of the 35S CaMV **promoter** and the synthetic Bt gene.

L15 ANSWER 6 OF 8 LIFESCI COPYRIGHT 2002 CSA DUPLICATE 2
ACCESSION NUMBER: 93:90504 LIFESCI
TITLE: Field performance of elite transgenic maize plants expressing an insecticidal protein derived from Bacillus thuringiensis .
AUTHOR: **Koziel, M.G.**; Beland, G.L.; Bowman, C.; Carozzi, N.B.; Crenshaw, R.; Crossland, L.; Dawson, J.; Desai, N.; Hill, M.; et al.
CORPORATE SOURCE: CIBA-GEIGY Agric. Biotechnol. Res. Unit, Res. Triangle Park, NC 27709, USA
SOURCE: BIO/TECHNOLOGY., (1993) vol. 11, no. 2, pp. 194-200.
ISSN: 0733-222X.
DOCUMENT TYPE: Journal
FILE SEGMENT: A
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We introduced a synthetic gene encoding a truncated version of the CryIA(b) protein derived from Bacillus thuringiensis into immature embryos of an elite line of maize using microprojectile bombardment. This gene was expressed using either the CaMV 35S **promoter** or a combination of two tissue specific promoters derived from maize. High levels of CryIA(b) protein were obtained using both **promoter** configurations. Hybrid maize plants resulting from crosses of transgenic elite inbred plants with commercial inbred lines were evaluated for resistance to European corn borer under field conditions. Plants expressing high levels of the insecticidal protein exhibited excellent resistance to repeated heavy infestations of this pest.

L15 ANSWER 7 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 93043043 MEDLINE
DOCUMENT NUMBER: 93043043 PubMed ID: 1285798
TITLE: Expression of a chimeric CaMV 35S Bacillus thuringiensis insecticidal protein gene in transgenic tobacco.
COMMENT: Erratum in: Plant Mol Biol 1993 Jan;21(2):413
AUTHOR: Carozzi N B; Warren G W; Desai N; Jayne S M; Lotstein R; Rice D A; Evola S; **Koziel M G**
CORPORATE SOURCE: CIBA-Geigy Agricultural Biotechnology Research Unit, Research Triangle Park, NC 27709.
SOURCE: PLANT MOLECULAR BIOLOGY, (1992 Nov) 20 (3) 539-48.
Journal code: A60; 9106343. ISSN: 0167-4412.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921201

AB Insecticidal transgenic tobacco plants containing a truncated Bacillus thuringiensis cryIA(b) crystal protein (ICP) gene expressed from the CaMV 35S **promoter** were analyzed for ICP gene expression under field and greenhouse conditions over the course of a growing season. We present new information on temporal and tissue-specific expression of a CaMV 35S/cryIA(b) gene. Levels of cryIA(b) protein and mRNA were compared in both homozygous and hemizygous lines throughout plant development. Levels of ICP mRNA and protein increased during plant development with a pronounced rise in expression at the time of flowering. Homozygous ICP lines produced higher levels of ICP than the corresponding hemizygous lines. ELISA analysis of different tissues in the tobacco plant showed ICP gene expression in most tissues with a predominance of ICP in older tissue. All transgenic ICP tobacco lines which were studied in the field and greenhouse contained 400 ng to 1 microgram ICP per gram fresh weight in leaves from the mid-section of the plant at flowering. The amounts of ICP produced by field lines were directly comparable to levels observed in greenhouse-grown plants.

L15 ANSWER 8 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 85159403 MEDLINE
DOCUMENT NUMBER: 85159403 PubMed ID: 6099400
TITLE: A cauliflower mosaic virus **promoter** directs expression of kanamycin resistance in morphogenic transformed plant cells.
AUTHOR: **Koziel M G**; Adams T L; Hazlet M A; Damm D; Miller J; Dahlbeck D; Jayne S; Staskawicz B J
SOURCE: JOURNAL OF MOLECULAR AND APPLIED GENETICS, (1984) 2 (6) 549-62.
Journal code: IZT; 8109497. ISSN: 0271-6801.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198504
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19980206
Entered Medline: 19850426

AB The **promoter** region of the CaMV inclusion body protein gene was modified for use in chimeric gene fusions. The modified **promoter** was used to construct a selectable marker for plant transformation based on the Tn 5 kanamycin resistance gene. This chimeric selectable marker was introduced into plant cells using oncogenic and deoncogenized strains of Agrobacterium tumefaciens. Both types of transformation produced kanamycin-resistant cell lines. The resistant cell lines derived from the deoncogenized strains were used to regenerate shoots. A second type of selection based on the ability of octopine synthase to detoxify aminoethyl cysteine was also used to select transformants in both oncogenic and nononcogenic transformation.

=> b medline caplus lifesci embase uspatfull biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

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FILE 'BIOSIS' ENTERED AT 15:18:51 ON 02 JAN 2002
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=> s hybrid (p) promoter

L1 13413 HYBRID (P) PROMOTER

=> s l1 and plant

L2 2364 L1 AND PLANT

=> s l2 and (ferrodoxin or ferrodoxine) and rold

L3 0 L2 AND (FERRODOXIN OR FERRODOXINE) AND ROLD

=> s l2 and (plastocyanin)

L4 2 L2 AND (PLASTOCYANIN)

=> dup rem l4

PROCESSING COMPLETED FOR L4
L5 2 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 ibib abs tot

L5 ANSWER 1 OF 2 USPATFULL
ACCESSION NUMBER: 2000:135033 USPATFULL
TITLE: Chimaeric gene coding for a transit peptide and a heterologous polypeptide
INVENTOR(S): Herrera-Estrella, Luis, Ghent, Belgium
Van Den Broeck, Guidi, Ghent, Belgium
Van Montagu, Marc, Brussels, Belgium
Schreier, Peter, Cologne, Germany, Federal Republic of
Schell, Josef, Cologne, Germany, Federal Republic of
Bohnert, Hans J., Tucson, AZ, United States

Cashomore, Anthony R., Woodside, NY, United States
Timko, Michael P., New York, NY, United States
Kausch, Albert P., Durham, NH, United States

PATENT ASSIGNEE(S): Plant Genetic Systems, Gent, Belgium (non-U.S. corporation)
Bayer AG, Leverkusen, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6130366		20001010
APPLICATION INFO.:	US 1997-984151		19971203 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-430257, filed on 28 Apr 1995, now patented, Pat. No. US 5728925 which is a continuation of Ser. No. US 1994-267306, filed on 29 Jun 1994, now abandoned which is a continuation of Ser.
No. US 1993-26213, filed on 1 Mar 1993, now abandoned which is a continuation of Ser. No. US 1991-794635, filed on 18 Nov 1991, now abandoned which is a continuation of Ser. No. US 1990-480343, filed on 14 Feb 1990, now abandoned which is a continuation of Ser.
No. US 1985-755173, filed on 15 Jul 1985, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1984-32757	19841228
	GB 1985-336	19850107

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fox, David T.
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Chimaeric DNA sequence which encodes: 1) a transmit peptide of a cytoplasmic precursor of a chloroplast protein or polypeptide of a **plant** and 2) a protein or polypeptide that is heterologous to the transit peptide. The chimaeric DNA sequence can be used as a vector for transforming a **plant** cell so that a chimaeric precursor of the heterologous protein or polypeptide is produced in the cytoplasm of the cell and the chimaeric precursor then transports the heterologous protein or polypeptide in vivo into a chloroplast of the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 2 USPATFULL
ACCESSION NUMBER: 1998:28301 USPATFULL
TITLE: Chimaeric gene coding for a transit peptide and a heterologous polypeptide
INVENTOR(S): Herrera-Estrella, Luis, Gent, Belgium
Van Den Broeck, Guido, Gent, Belgium
Van Montagu, Marc, Brussel, Belgium
Schreier, Peter, Cologne, Germany, Federal Republic of
Schell, Jeff, Cologne, Germany, Federal Republic of
Bohnert, Hans J., Tucson, AZ, United States
Cashmore, Anthony R., Woodside, NY, United States
Timko, Michael P., New York, NY, United States
Kausch, Albert P., Durham, NH, United States
PATENT ASSIGNEE(S): Plant Genetic Systems, N.V., Brussels, Belgium (non-U.S. corporation)
Bayer A.G., Leverkusen, Germany, Federal Republic of

(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5728925		19980317
APPLICATION INFO.:	US 1995-430257		19950428 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-267306, filed on 29 Jun 1994, now abandoned which is a continuation of Ser. No. US 1993-26213, filed on 1 Mar 1993, now abandoned which is a continuation of Ser. No. US 1991-794635, filed on 18 Nov 1991, now abandoned which is a continuation of Ser. No. US 1990-480343, filed on 14 Feb 1990, now abandoned which is a continuation of Ser. No. US 1985-755173, filed on 15 Jul 1985, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1984-32757	19841228
	GB 1985-336	19850107

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fox, David T.
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2068
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Chimaeric DNA sequence which encodes: 1) a transit peptide of a cytoplasmic precursor of a chloroplast protein or polypeptide of a **plant** and 2) a protein or polypeptide that is heterologous to the transit peptide. The chimaeric DNA sequence can be used as a vector for transforming a **plant** cell so that a chimaeric precursor of the heterologous protein or polypeptide is produced in the cytoplasm of the cell and the chimaeric precursor then transports the heterologous protein or polypeptide in vivo into a chloroplast of the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s l2 and (adenosyl and methionine)

L6 22 L2 AND (ADENOSYL AND METHIONINE)

=> dup rem l6

PROCESSING COMPLETED FOR L6
L7 22 DUP REM L6 (0 DUPLICATES REMOVED)

=> d l7 ibib abs tot

L7 ANSWER 1 OF 22 USPATFULL
ACCESSION NUMBER: 2001:214858 USPATFULL
TITLE: Methods for modifying the production of a polypeptide
INVENTOR(S): Brody, Howard, Davis, CA, United States
Yaver, Deborah S., Davis, CA, United States
Lamsa, Michael, Davis, CA, United States
Hansen, Kim, Vaerlose, Denmark
PATENT ASSIGNEE(S): Novozymes Biotech, Inc, Davis, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6223002	B1	20011127
APPLICATION INFO.:	US [redacted]9-339972		19990625 (9[redacted]

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-928692, filed on 12 Sep 1997, now patented, Pat. No. US 5958727, issued on 28 Sep 1999 Continuation-in-part of Ser. No. US 1996-713312, filed on 13 Sep 1996, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Guzo, David
ASSISTANT EXAMINER: Leffeis, Jr., Gerald G.
LEGAL REPRESENTATIVE: Starnes, Robert L.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 46 Drawing Figure(s); 46 Drawing Page(s)
LINE COUNT: 4259
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for modifying the production of a polypeptide, comprising: (a) introducing a nucleic acid construct into a cell, wherein the cell comprises a DNA sequence encoding a polypeptide, under conditions in which the nucleic acid construct integrates into the genome of the cell at a locus not within the DNA sequence encoding the polypeptide to produce a mutant cell, wherein the integration of the nucleic acid construct modifies the production of the polypeptide by the mutant cell relative to the cell when the mutant cell and the cell are cultured under the same conditions; and (b) identifying the mutant cell with the modified production of the polypeptide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 22 USPATFULL
ACCESSION NUMBER: 2001:116808 USPATFULL
TITLE: DNA encoding methymycin and pikromycin
INVENTOR(S): Sherman, David H., St. Louis Park, MN, United States
Liu, Hung-Wen, Roseville, MN, United States
Xue, Yongquan, St. Paul, MN, United States
Zhao, Lishan, St. Paul, MN, United States
PATENT ASSIGNEE(S): Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6265202	B1	20010724
APPLICATION INFO.:	US 1998-105537		19980626 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Nashed, Nashaat T.
LEGAL REPRESENTATIVE: Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 160 Drawing Figure(s); 158 Drawing Page(s)
LINE COUNT: 3335
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel pathway for the synthesis of polyhydroxyalkanoates is provided. A method of synthesizing a recombinant polyhydroxyalkanoate monomer synthase is also provided. These recombinant polyhydroxyalkanoate synthases are derived from multifunctional fatty acid synthases or polyketide synthases and generate hydroxyacyl acids capable of polymerization by a polyhydroxyalkanoate synthase. Also provided is a biosynthetic gene cluster for methymycin and pikomycin as well as a biosynthetic gene cluster for desosamine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 22 USPATFULL

ACCESSION NUMBER: 2001:44438 USPATFULL
TITLE: Control of fruit ripening through genetic control of ACC synthase synthesis
INVENTOR(S): Theologis, Athanasios, Los Altos Hills, CA, United States
Sato, Takahido, Tokyo, Japan
PATENT ASSIGNEE(S): The United States of America as represented by the Department of Agriculture, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6207881	B1	20010327
APPLICATION INFO.:	US 1995-378313		19950125 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-862493, filed on 19 Apr 1992, now abandoned Continuation-in-part of Ser. No. US 1990-579896, filed on 10 Sep 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Chereskin, Che S.
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 45 Drawing Figure(s); 39 Drawing Page(s)
LINE COUNT: 1633
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant materials for the production of tomato ACC synthase are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 22 USPATFULL

ACCESSION NUMBER: 2000:164712 USPATFULL
TITLE: Control of fruit ripening through genetic control of ACC synthase synthesis
INVENTOR(S): Theologis, Athanasios, Los Altos Hills, CA, United States
Sato, Takahido, Funabash, Japan
PATENT ASSIGNEE(S): The United States of America as represented by the United States Department of Agriculture, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6156956		20001205
APPLICATION INFO.:	US 1998-33349		19980302 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-481171, filed on 7 Jun 1995, now patented, Pat. No. US 5723766 which is a division of Ser. No. US 1995-378313, filed on 25 Jan 1995, now patented, Pat. No. US 5824860 which is a continuation of Ser. No. US 1992-862493, filed on 2 Apr 1992, now abandoned which is a continuation-in-part of Ser. No. US 1990-579896, filed on 10 Sep 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Nelson, Amy J.
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 24

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 43 Drawing Figure(s); 38 Drawing Pages)
LINE COUNT: 371

AB ACC synthases of higher plants are coded by multigene families; only certain members of these families are responsible for various **plant** development characteristics effected by ethylene. Control of the processes in plants which are mediated by ACC synthase, such as fruit ripening, can be effected by controlling expression of the relevant ACC synthase gene. In addition, comparison of the amino acid and nucleotide sequence of the ACC synthases from cucumber and tomato provides consensus sequences that permit the design of PCR primers that permit the isolation of ACC synthases from a variety of higher plants.

L7 ANSWER 5 OF 22 USPATFULL
ACCESSION NUMBER: 2000:121692 USPATFULL
TITLE: Synthetic **hybrid** tomato E4/E8 **plant promoter**
INVENTOR(S): Bestwick, Richard K., Portland, OR, United States
Kellogg, Jill Anne, Portland, OR, United States
PATENT ASSIGNEE(S): Agritope, Inc., Portland, OR, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6118049		20000912
APPLICATION INFO.:	US 1998-157077		19980918 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-59234	19970918 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Nelson, Amy J.
LEGAL REPRESENTATIVE: Judge, Linda R.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 9
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 1730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a synthetic **hybrid promoter** composed of polynucleotide segments derived from the E8 and E4 gene promoters. The **hybrid promoter** is capable of providing high-level expression of heterologous genes, particularly in transformed fruit. DNA constructs containing the E8-E4 **hybrid promoter** operably linked to an exemplary heterologous SAMase gene are effective in conferring a delayed ripening phenotype to transformed fruit.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 22 USPATFULL
ACCESSION NUMBER: 2000:106060 USPATFULL
TITLE: Tumor suppressor gene, HIC-1
INVENTOR(S): Baylin, Stephen B., Baltimore, MD, United States
Wales, Michele Makos, Rockville, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6103877		20000815
APPLICATION INFO.:	US 1998-85407		19980526 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-340203, filed on 15 Nov 1994, now patented, Pat. No. US 5756668
DOCUMENT TYPE: Utility

FILE SEGMENT: Granted
PRIMARY EXAMINER: McKelvey, Terry
LEGAL REPRESENTATIVE: Gray Cary Ware & Freidenrich LLP, Hall, Lisa A.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1956
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polynucleotide and polypeptide sequences encoding a novel tumor suppressor, HIC-1, are provided. Also included is a method for detecting a cell proliferative disorder associated with HIC-1. HIC-1 is a marker which can be used diagnostically, prognostically and therapeutically over the course of such disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 22 USPATFULL
ACCESSION NUMBER: 2000:98211 USPATFULL
TITLE: Human nucleic acid methylases
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Lal, Preeti, Santa Clara, CA, United States
Corley, Neil C., Mountain View, CA, United States
Guegler, Karl J., Menlo Park, CA, United States
Yue, Henry, Sunnyvale, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6096526		20000801	
APPLICATION INFO.:	US 1998-82310		19980520	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Carlson, Karen Cochrane
ASSISTANT EXAMINER: Srivastava, Devesh
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 2590
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a human nucleic acid methylases (HNAM) and polynucleotides which identify and encode HNAM. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HNAM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 22 USPATFULL
ACCESSION NUMBER: 2000:57545 USPATFULL
TITLE: Human transferases
INVENTOR(S): Lal, Preeti, Santa Clara, CA, United States
Bandman, Olga, Mountain View, CA, United States
Hillman, Jennifer L., Mountain View, CA, United States
Guegler, Karl J., Menlo Park, CA, United States
Gorgone, Gina A., Boulder Creek, CA, United States
Corley, Neil C., Mountain View, CA, United States
Patterson, Chandra, Mountain View, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6060250		20000509

APPLICATION INFO.: US 1998-109204 19980630 (9)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prouty, Rebecca E.
LEGAL REPRESENTATIVE: Muenzen, Colette C.Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 3615
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides three human transferases (HUTRAN) and polynucleotides which identify and encode HUTRAN. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HUTRAN.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 22 USPATFULL
ACCESSION NUMBER: 1999:117299 USPATFULL
TITLE: Methods for modifying the production of a polypeptide
INVENTOR(S): Brody, Howard, Davis, CA, United States
Yaver, Deborah S., Davis, CA, United States
Lamsa, Michael, Davis, CA, United States
Hansen, Kim, Vaerlose, Denmark
PATENT ASSIGNEE(S): Novo Nordisk Biotech, Inc, Davis, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5958727		19990928
APPLICATION INFO.:	US 1997-928692		19970912 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-713312, filed on 13 Sep 1996, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ketter, James
ASSISTANT EXAMINER: Yucel, Irem
LEGAL REPRESENTATIVE: Zelson, Steve T., Lambiris, Elias J., Starnes, Robert L.
NUMBER OF CLAIMS: 53
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 38 Drawing Figure(s); 46 Drawing Page(s)
LINE COUNT: 6123
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods for modifying the production of a polypeptide, comprising: (a) introducing a nucleic acid construct into a cell, wherein the cell comprises a DNA sequence encoding a polypeptide, under conditions in which the nucleic acid construct integrates into the genome of the cell at a locus not within the DNA sequence encoding the polypeptide to produce a mutant cell, wherein the integration of the nucleic acid construct modifies the production of the polypeptide by the mutant cell relative to the cell when the mutant cell and the cell are cultured under the same conditions; and (b) identifying the mutant cell with the modified production of the polypeptide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 22 USPATFULL
ACCESSION NUMBER: 1999:110534 USPATFULL
TITLE: Nucleic acid molecules encoding cytochrome P450-type

proteins involved in the brassinosteroid synthesis in plan[redacted]

INVENTOR(S): Kon[redacted] Csaba, Koln, Germany, Federal [redacted]public of
Mathur, Jaideep, Koln, Germany, Federal Republic of
Szekeres, Miklos, Szeged, Germany, Federal Republic of
Altmann, Thomas, Berlin, Germany, Federal Republic of

PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., Berlin, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5952545		19990914
APPLICATION INFO.:	US 1996-622166		19960327 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Smith, Lynette F.
ASSISTANT EXAMINER: Haas, Thomas
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1,10,11
NUMBER OF DRAWINGS: 25 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 1865
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention describes nucleic acid molecules encoding cytochrome P450-t proteins involved in the brassionosteroid synthesis in plants, transgenic **plant** cells and plants containing such nucleic acid molecules as well as processes for the identification of other proteins involved in brassinosteroid synthesis and processes for the identification of substances acting as brassinosteroids or as brassinosteroid inhibitors in plants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 22 USPATFULL
ACCESSION NUMBER: 1999:78595 USPATFULL
TITLE: Tumor suppressor gene, HIC-1
INVENTOR(S): Baylin, Stephen B., Baltimore, MD, United States
Wales, Michele Makos, Rockville, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5922590		19990713
APPLICATION INFO.:	US 1995-452427		19950525 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-340203, filed on 15 Nov 1994		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Lathrop, Brian
LEGAL REPRESENTATIVE: Fish & Richardson, P.C.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Polynucleotide and polypeptide sequences encoding a novel tumor suppressor, HIC-1 , are provided. Also included is a method for detecting a cell proliferative disorder associated with HIC-1. HIC-1 is a marker which can be used diagnostically, prognostically and therapeutically over the course of such disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 22 USPATFULL

ACCESSION NUMBER:	1999:27458 USPATFULL
TITLE:	Hu[redacted] S-**adenosyl**-L-**methionine** methyltransferase
INVENTOR(S):	Bandman, Olga, Mountain View, CA, United States Lal, Preeti, Sunnyvale, CA, United States Corley, Neil C., Mountain View, CA, United States Shah, Purvi, Sunnyvale, CA, United States
PATENT ASSIGNEE(S):	Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5876996		19990302
APPLICATION INFO.:	US 1997-900565		19970725 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Prouty, Rebecca E.
ASSISTANT EXAMINER:	Stole, Einar
LEGAL REPRESENTATIVE:	Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS:	9
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT:	2244

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a human S-**adenosyl**-L-**methionine** methyltransferase (SAM-MT) and polynucleotides which identify and encode SAM-MT. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of SAM-MT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 13 OF 22 USPATFULL

ACCESSION NUMBER:	1998:162294 USPATFULL
TITLE:	Polynucleotides encoding human S-**adenosyl** -5-homocysteine hydrolase derived from bladder
INVENTOR(S):	Hillman, Jennifer L., Mountain View, CA, United States Corley, Neil C., Mountain View, CA, United States Lal, Preeti, Santa Clara, CA, United States Shah, Purvi, Sunnyvale, CA, United States
PATENT ASSIGNEE(S):	Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5854023		19981229
APPLICATION INFO.:	US 1997-896005		19970717 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Carlson, Karen Cochrane
LEGAL REPRESENTATIVE:	Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT:	2375

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a human S-**adenosyl**-5-homocysteine hydrolase (SAHH) and polynucleotides which identify and encode SAHH. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of SAHH.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 14 OF 22 USPATFULL
ACCESSION NUMBER: 19[redacted]154030 USPATFULL
TITLE: Tumor suppressor gene, HIC-1
INVENTOR(S): Baylin, Stephen B., Baltimore, MD, United States
Wales, Michele Makos, Rockville, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5846712		19981208
APPLICATION INFO.:	US 1995-452567		19950525 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-340203, filed on 15 Nov 1994
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Zitomer, Stephanie W.
ASSISTANT EXAMINER: Atzel, Amy
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1664
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polynucleotide and polypeptide sequences encoding a novel tumor suppressor, HIC-1, are provided. Also included is a method for detecting a cell proliferative disorder associated with HIC-1. HIC-1 is a marker which can be used diagnostically, prognostically and therapeutically over the course of such disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 15 OF 22 USPATFULL
ACCESSION NUMBER: 1998:58089 USPATFULL
TITLE: Hypermethylated in cancer polypeptide, HIC-1
INVENTOR(S): Baylin, Stephen B., Baltimore, MD, United States
Wales, Michele Makos, Rockville, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5756668		19980526
APPLICATION INFO.:	US 1994-340203		19941115 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fleisher, Mindy
ASSISTANT EXAMINER: McKelvey, Terry A.
LEGAL REPRESENTATIVE: Fish and Richardson P.C.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1725
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polynucleotide and polypeptide sequences encoding a novel tumor suppressor, HIC-1, are provided. Also included is a method for detecting a cell proliferative disorder associated, with HIC-1. HIC-1 is a marker which can be used diagnostically, prognostically and therapeutically over the course of such disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 16 OF 22 USPATFULL

ACCESSION NUMBER: 1998:22519 USPATFULL
TITLE: Control of fruit ripening through genetic control of ACC synthase synthesis
INVENTOR(S): Theologis, Athanasios, Los Altos Hills, CA, United States
Sato, Takahido, Tokyo, Japan
PATENT ASSIGNEE(S): The United States of America as represented by the Secretary of the Agriculture, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5723766		19980303
APPLICATION INFO.:	US 1995-481171		19950607 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-378313, filed on 25 Jan 1995 which is a continuation of Ser. No. US 1992-862493, filed on 2 Apr 1992, now abandoned which is a continuation-in-part of Ser. No. US 1990-579896, filed on 10 Sep 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Chereskin, Che S.
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 9
NUMBER OF DRAWINGS: 45 Drawing Figure(s); 39 Drawing Page(s)
LINE COUNT: 2149
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB ACC synthases of higher plants are coded by multigene families; only certain members of these families are responsible for various **plant** development characteristics effected by ethylene. Control of the processes in plants which are mediated by ACC synthase can be effected by controlling expression of the relevant ACC synthase gene. In addition, comparison of the amino acid and nucleotide sequence of the ACC synthases from cucumber and tomato provides consensus sequences that permit the design of PCR primers that permit the isolation of ACC synthases from a variety of higher plants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:763350 CAPLUS
DOCUMENT NUMBER: 126:101772
TITLE: Tissue-specific expression conferred by the S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar
AUTHOR(S): Mijnsbrugge, Kristine Vander; Van Montagu, Marc; Inze, Dirk; Boerjan, Wout
CORPORATE SOURCE: Lab. Genetica, Dep. Genetics, Flanders Interuniv. Inst. Biotechnol., Univ. Gent, Ghent, B-9000, Belg.
SOURCE: Plant Cell Physiol. (1996), 37(8), 1108-1115
CODEN: PCPHA5; ISSN: 0032-0781
PUBLISHER: Japanese Society of Plant Physiologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Arabidopsis the promoter of the gene encoding S-**adenosyl**-L-**methionine** synthetase (SAM-S) Psam-1 confers expression preferentially in the vascular tissue. In search for promoters that drive expression in particular cells of the lignifying tissues in trees, we have analyzed the expression pattern conferred by the Psam-1 promoter in transgenic poplar. Histochem. analyses demonstrated .beta.-glucuronidase

(GUS) activity mainly in phloem and cortex tissue throughout the **plant**, and in root tips. Fluorimetric assays showed high GUS activity in the tissue outside (phloem, cortex and co[redacted] compared to those inside (xylem and pith) of the cambial layer. In contrast, the endogenous SAM-S activity was high in tissues inside and low in tissues outside of the cambial layer. RNA gel blot anal. demonstrated a high transcript level of the endogenous sam-s gene(s) in tissues both outside and inside the cambial layer. This indicates that the low SAM-S activity in the bark was at least partially due to translational and/or pos-translational regulation of the endogenous sam-s gene(s). In dormant transgenics, the tissue specificity was conserved, but the activity levels were up to 10-fold reduced.

L7 ANSWER 18 OF 22 USPATFULL

ACCESSION NUMBER: 95:92697 USPATFULL
TITLE: DNA encoding 85kd polypeptide useful in diagnosis of Mycoplasma infections in animals
INVENTOR(S): Kuner, Jerry, Longmont, CO, United States
Ko, Christine, Boulder, CO, United States
PATENT ASSIGNEE(S): Synergen, Inc., Boulder, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5459048		19951017
APPLICATION INFO.:	US 1993-153495		19931117 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-962075, filed on 16 Oct 1992, now abandoned which is a continuation of Ser. No. US 1990-502640, filed on 2 Apr 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-196891, filed on 18 May 1988, now abandoned which is a continuation of Ser. No. US 1986-889153, filed on 25 Jul 1986, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lacey, David L.
ASSISTANT EXAMINER: Nisbet, T. Michael
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 39 Drawing Figure(s); 39 Drawing Page(s)
LINE COUNT: 2298
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A class of polypeptides useful in an in vitro diagnosis of Mycoplasma infection in animals is disclosed. These polypeptides are also capable of inducing an immune response in swine which were previously not exposed to Mycoplasma. Recombinant DNA methods for the production of these polypeptides and certain phage vectors and DNA sequences useful in these methods are also disclosed. Methods of vaccinating animals utilizing a vaccination composition which includes these polypeptides is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 22 USPATFULL

ACCESSION NUMBER: 95:54315 USPATFULL
TITLE: Minactivin compositions and antibodies to minactivin
INVENTOR(S): Antalis, Toni M., Drummoyne, Australia
Barnes, Thomas M., Lane Cove, Australia
Clark, Michelle A., Greenwich, Australia
Devine, Peter L., Gladesville, Australia
Goss, Neil H., Wahroonga, Australia

Lehrbach, Philip R., Wahroonga, Australia
PATENT ASSIGNEE(S): Biotechnology Australia, Pty., Ltd., New South Wales, Australia (non-U.S. corporation)
Australian National University, Acton, Australia (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5426044		19950620
APPLICATION INFO.:	US 1991-693636		19910430 (7)

DISCLAIMER DATE: 20120606
RELATED APPLN. INFO.: Division of Ser. No. US 1987-25815, filed on 13 Mar 1987, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	AU 1986-5017	19860313
	AU 1986-6033	19860522
	AU 1986-8100	19860918
	AU 1986-9104	19861121

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Schmickel, David
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 31 Drawing Page(s)
LINE COUNT: 1902
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel human protein, minactivin, can be produced by recombinant DNA technology, Biologically active native minactivin, peptides derived from minactivin, and their amino acid sequences can also be purified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 20 OF 22 USPATFULL
ACCESSION NUMBER: 95:49915 USPATFULL
TITLE: Human PAI-2
INVENTOR(S): Stephens, Ross W., Oslo, Norway
Golder, Jeffrey P., Mona Vale, Australia
Antalis, Toni M., Toowong, Australia
Barnes, Thomas M., Boston, MA, United States
Clark, Michell A., Crows Nest, Australia
Devine, Peter L., Helensvale, Australia
Goss, Neil H., Wahroonga, Australia
Lehrbach, Philip R., Wahroonga, Australia
PATENT ASSIGNEE(S): Biotechnology Australia, Pty., Ltd., New South Wales, Australia (non-U.S. corporation)
Australian National University, Acton, Australia (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5422090		19950606
APPLICATION INFO.:	US 1992-911531		19920715 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1991-765495, filed on 26 Sep 1991, now abandoned And Ser. No. US 1991-693542, filed on 30 Apr 1991, now abandoned which is a division of Ser. No. US 1987-25815, filed on 13 Mar 1987, now abandoned , said Ser. No. US -765495 which is a continuation of Ser. No. US 1986-860336, filed on 13 Jun 1986, now abandoned

	NUMBER	DATE

PRIORITY INFORMATION:	AU 1984-6531	19840813
	AU 1986-5017	19860313
	AU 1986-6033	19860522
	AU 1986-8100	19860918
	AU 1986-9104	19861121

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schwartz, Richard A.
ASSISTANT EXAMINER: Brown, Gary L.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 72 Drawing Figure(s); 60 Drawing Page(s)
LINE COUNT: 3634
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Minactivin (also known as Plasminogen Activator Inhibitor-2 [PAI-2]), a protein inactivator of urokinase-type plasminogen activator, has been shown to be a natural inactivator of this plasminogen activator which is associated with invasive tumors, and is therefore indicated as a crucial element in the body's normal defense against tumor invasion and metastasis. It may be produced by the cultivation of minactivin-producing cells in vitro, and recovery of the cell culture supernatant. By controlling the culture conditions, the protein minactivin may be produced in a partially purified form which may be used for diagnosis and treatment of tumors. The specification discloses purification of biologically active native minactivin, as well as peptides derived from minactivin and their amino acid sequences. The specification also discloses methods for production of PAI-2 by recombinant DNA technology, characterization of a PAI-2 gene sequence, and expression and purification of large quantities of biologically active PAI-2 from a recombinant host.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 21 OF 22 USPATFULL
ACCESSION NUMBER: 94:39986 USPATFULL
TITLE: Glyphosate-tolerant 5-enolpyruvyl-3-phosphoshikimate synthases
INVENTOR(S): Eichholtz, David A., St. Louis, MO, United States
Gasser, Charles S., Chesterfield, MO, United States
Kishore, Ganesh M., Chesterfield, MO, United States
PATENT ASSIGNEE(S): Monsanto Company, St. Louis, MO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5310667		19940510
APPLICATION INFO.:	US 1989-380963		19890717 (7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Chereskiin, Che S.
LEGAL REPRESENTATIVE: Hoerner, Jr., Dennis R., Shear, Richard H.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2322
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Glyphosate-tolerant 5-enolpyruvyl-3-phosphoshikimate (EPSP) synthases, DNA encoding glyphosate-tolerant EPSP synthases, **plant** genes encoding the glyphosate-tolerant enzymes, **plant** transformation vectors containing the genes, transformed **plant** cells and differentiated transformed plants containing the **plant** genes are disclosed. The glyphosate-tolerant EPSP synthases are prepared by

substituting an alanine residue for a glycine residue in a first conserved sequence found between positions 80 and 120 and either an aspartic acid residue or asparagine residue for a glycine residue in a second conserved sequence found between positions 120 and 160 in the mature wild type EPSP synthase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 22 OF 22 USPATFULL

ACCESSION NUMBER:	91:104100 USPATFULL
TITLE:	Interleukin-1 inhibitors
INVENTOR(S):	Hannum, Charles H., Boulder, CO, United States Eisenburg, Stephen P., Boulder, CO, United States Thompson, Robert C., Boulder, CO, United States Arend, William P., Denver, CO, United States Joslin, Fenneke G., Denver, CO, United States
PATENT ASSIGNEE(S):	Synergen, Inc., Boulder, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5075222		19911224
APPLICATION INFO.:	US 1990-506522		19900406 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1988-266531, filed on 3 Nov 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-248521, filed on 23 Sep 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-238713, filed on 31 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-199915, filed on 27 May 1988, now abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Schwartz, Richard A.
ASSISTANT EXAMINER:	Ellis, Joan
LEGAL REPRESENTATIVE:	Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS:	31
EXEMPLARY CLAIM:	17
NUMBER OF DRAWINGS:	26 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT:	1615

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB DNA sequences that encode Interleukin-1 inhibitors and recombinant-DNA methods for the production of interleukin-1 inhibitors are provided. The DNA sequences encode proteins having interleukin-1 inhibitors activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L7 ANSWER 5 OF 22 USPATFULL

ACCESSION NUMBER:	2000:121692 USPATFULL
TITLE:	Synthetic **hybrid** tomato E4/E8 **plant promoter**
INVENTOR(S):	Bestwick, Richard K., Portland, OR, United States Kellogg, Jill Anne, Portland, OR, United States
PATENT ASSIGNEE(S):	Agritope, Inc., Portland, OR, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6118049		20000912
APPLICATION INFO.:	US 1998-157077		19980918 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US [redacted]97-59234	19970918 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Nelson, Amy J.
LEGAL REPRESENTATIVE: Judge, Linda R.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 9
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 1730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Synthetic **hybrid** tomato E4/E8 **plant promoter**

AB The present invention is directed to a synthetic **hybrid** **promoter** composed of polynucleotide segments derived from the E8 and E4 gene promoters. The **hybrid promoter** is capable of providing high-level expression of heterologous genes, particularly in transformed fruit. DNA constructs containing the E8-E4 **hybrid promoter** operably linked to an exemplary heterologous SAMase gene are effective in conferring a delayed ripening phenotype to transformed fruit.

SUMM The present invention relates to a synthetic E8-E4 **hybrid** **promoter** composed of polynucleotide segments derived from the tomato E8 and tomato E4 genes, and to DNA constructs, chimeric genes, vectors, kits, and transformation methods employing the **promoter** .

SUMM Adams, D. O., and Yang, S. F., **Plant** Physiology 70:117-123 (1977).
SUMM Becker, D., et al., **Plant** Mol. Biol. 20:1195-1197 (1992).
SUMM Cordes, S., et al., The **Plant** Cell 1:1025-1034 (1989).
SUMM Coupe, S. A. and Deikman, J., The **Plant** Journal 11(6):1207-1218 (1997).
SUMM Deikman, J., et al., **Plant** Physiol. 100(4):2013-2017 (1992).
SUMM Fang, G., and Grumet, R., **Plant** Cell Rep. 9:160-164 (1990).
SUMM Good, X., et al., **Plant** Mol. Biol. 26:781-790 (1994).
SUMM Jefferson, R. A., **Plant** Mol. Biol. Rep. 5:387 (1987b).
SUMM Jefferson, R. A., **Plant** Mol. Biol. Rep. 5:387 (1987b).
SUMM Klee, H. J., et al., **Plant** Cell 3:1187-1193 (1991).
SUMM Knessl, M. L. and Deikman, J., **Plant** Physiology 112:537-547 (1996).
SUMM Kramer, M. G., et al., in BIOLOGY & BIOTECHNOLOGY OF THE **PLANT** HORMONE ETHYLENE Kluwer Academic Publishers, The Netherlands (1996).
SUMM Lin, E., et al., **Plant** Mol. Biol. 23:489-499 (1993).
SUMM Melchers, L. S., et al., **Plant** J. 5:469-480 (1994).
SUMM Miki, B. L. A., et al., **PLANT** DNA INFECTIOUS AGENTS (Hohn, T., et al., Eds.) Springer-Verlag, Vienna, Austria, pp. 249-265 (1987).
SUMM Montgomery, J., et al., **Plant** Cell 5:1049-1062 (1993).
SUMM Ni, M., et al., **Plant** J. 7:661-676 (1995).
SUMM Odell, J. T., et al., **Plant** Mol Biol 10(3):263-272 (1988).
SUMM Penarrubia, L., et al., **Plant** Cell 4:681-687 (1992).
SUMM Picton, S., et al., **Plant** Physiology 103(4):1471-1472 (1993).
SUMM Ponstein, A. S., et al., **Plant** Physiol. 104:109-118 (1994).
SUMM Toubart, P., et al., **Plant** J. 3:367-373 (1992).
SUMM Valles, M. P. and Lasa, J. M., **Plant** Cell Rep. 13:145-148 (1994).
SUMM Van Haaren, M. J. J., et al., **Plant** Mol. Bio. 21:625-640 (1993).
SUMM Woloshuk, C. P., et al., J. **Plant** Cell 3:619-628 (1991).
SUMM Xu, R., et al., **Plant** Mol. Biol. 31:1117-1127 (1996).
SUMM Zhu, Q., et al., **Plant** Cell 7:1681-1689 (1995).

SUMM Promoters that regulate gene expression in plants are essential elements of **plant** genetic engineering. Several examples of promoters useful for the expression of selected genes in plants are now available (Zhu, et. . .

SUMM . . . plants has typically involved the use of constitutive

promoters, i.e., promoters which drive the expression of a product throughout the **plant** at all times and in most tissues.

SUMM **Plant** promoters (promoters derived from **plant** sources) effective to provide constitutive expression, are less well known, and include hsp80, Heat Shock Protein 80 from cauliflower, (Brunke. . . et al., 1993). These promoters can be used to direct the constitutive expression of heterologous nucleic acid sequences in transformed **plant** tissues.

SUMM . . . the present invention include a region of DNA that regulates transcription of the immediately adjacent (downstream) gene to a specific **plant** tissue. According to methods of the present invention, heterologous genes are linked to the promoters of the present invention. Exemplary. . .

SUMM At present, a relatively small number of **plant** promoters, particularly constitutive **plant** promoters, have been identified. The use of such promoters in **plant** genetic engineering has been rather limited to date, since gene expression in plants is, for the most part, typically tissue,. . .

SUMM A need exists for tissue and developmental stage specific promoters that are functional in **plant** cells, and which are capable of providing high level expression of heterologous genes.

SUMM The present invention is directed to a synthetic **promoter** composed of a combination of cis-acting elements derived from the transcriptional regulatory sequences of the E8 and E4 genes, as exemplified by tomato. The synthetic **hybrid promoter** allows high-level, fruit specific expression of nucleic acid sequences placed under its control.

SUMM . . . one aspect, the invention provides a DNA construct which contains a DNA coding sequence under the transcriptional control of a **hybrid** E8-E4 **promoter**. The DNA coding sequence is typically heterologous to the **hybrid promoter** and is operably linked to the **promoter** to enable expression of the product. Exemplary products include, but are not limited to S-adenosylmethionine hydrolase (SAMase), amino-cyclopropane-1-carboxylic acid (ACC). . .

SUMM The E8-E4 **hybrid promoter** of the invention is composed of a polynucleotide segment derived from an E8 gene **promoter** which is fused to a polynucleotide segment derived from an E4 gene **promoter** positioned downstream of the E8 **promoter** segment. The E8 **promoter**-derived polynucleotide segment includes at least 30 contiguous nucleotides selected from the region extending from nucleotide positions -2257 to -847 of the tomato E8 **promoter** which corresponds to approximately nucleotides 1 to 1411 of SEQ ID NO:7, or the functional equivalent thereof. The polynucleotide segment derived from an E4 gene **promoter** includes at least 200 contiguous nucleotides selected from the region extending from nucleotide positions -1150 to +16 of the tomato E4 **promoter** which corresponds to approximately nucleotides 271 to 1437 of SEQ ID NO:8, or the functional equivalent thereof. The particular combination of E8 and E4 polynucleotide segments produces a **hybrid promoter** which is effective to drive expression of a heterologous gene (e.g., a reporter gene) at a level of at least about 75-300% of the expression level obtained using either an unmodified E4 or E8 gene **promoter**.

SUMM In one embodiment of the **hybrid promoter**, the nucleotide sequence of the E8 **promoter** segment corresponds to nucleotides -1529 to -847 of the tomato E8 **promoter**, or the functional equivalent thereof, which corresponds to approximately nucleotides 3 to 686 of SEQ ID NO:6 and nucleotides 729 to 1411 of SEQ ID NO:7. The **hybrid promoter** also contains an E4 **promoter** segment corresponding to nucleotides -315 to +16 of the

tomato E4 **promoter**, or the functional equivalent thereof, which corresponds to approximately nucleotides 693 to 1023 of SEQ ID 6 or nucleotides 1107 to 1437 of SEQ ID NO:8, referred herein as the "short E8-E4 **hybrid promoter**".

SUMM In another embodiment of the **hybrid promoter**, the nucleotide sequence of the E8 **promoter** segment corresponds to nucleotides -2257 to -1103 of the tomato E8 **promoter**, or the functional equivalent thereof, which corresponds to approximately nucleotides 1 to 1160 of SEQ ID NO:1 and nucleotides 1 to 1156 of SEQ ID NO:7. The **hybrid promoter** also contains an E4 **promoter** segment corresponding to nucleotides -1150 to +16 of the tomato E4 **promoter**, or the functional equivalent thereof, which corresponds to approximately nucleotides 1157 to 2323 of SEQ ID 1 or nucleotides 271 to 1437 of SEQ ID NO:8, designated herein as the "long E8-E4 **promoter**".

SUMM In one respect, the E8-E4 **hybrid promoter** of the present invention can be used to reduce ethylene production in transformed fruit cells, to thereby alter the ripening. . .

SUMM The present invention also includes the use of any of the above chimeric gene constructs to generate a **plant** transformation vector. Such vectors can be used in any **plant** cell transformation method, including Agrobacterium-based methods, electroporation, microinjection, and microprojectile bombardment. These vectors may form part of a **plant** transformation kit. Other components of the kit may include, but are not limited to, reagents useful for **plant** cell transformation.

SUMM In another embodiment, the invention includes a **plant** cell, **plant** tissue, transgenic **plant**, fruit cell, whole fruit, seeds or calli containing any of the above-described chimeric genes and the corresponding expressed gene products.. . .

SUMM . . . present invention, the hybrid promoters described herein are employed in a method for delaying ripening of fruit from a fruit-bearing **plant**. In this method, a transgenic **plant** containing the chimeric gene of the present invention is grown to produce a transgenic **plant** bearing fruit. In one particular embodiment, the chimeric gene encodes a product capable of reducing ethylene biosynthesis when expressed in **plant** cells (e.g., S-**adenosyl-methionine** hydrolase, amino-cyclopropane-1-carboxylic acid (ACC) deaminase, ACC oxidase antisense molecule, ACC synthase antisense molecule, ACC oxidase cosuppression molecule, ACC synthase cosuppression. . .

SUMM Further, the invention includes a method for producing a transgenic **plant** such as a fruit-bearing **plant**. In this method, the chimeric gene of the present invention, typically carried in an expression vector allowing selection in **plant** cells, is introduced into progenitor cells of selected **plant**. These progenitor cells are then grown to produce a transgenic **plant** bearing fruit.

SUMM Yet another aspect of the invention is directed to a method for conferring enhanced expression activity to an E4 **promoter**. In the method, a polynucleotide segment of at least 30 contiguous nucleotides selected from the region extending from nucleotide positions. . . to 1411 of SEQ ID NO:7, or the functional equivalent thereof, is fused in an upstream orientation to an E4 **promoter** polynucleotide segment of at least 200 contiguous nucleotides selected from the region extending from nucleotide positions -1150 to +16 of. . . which corresponds to approximately nucleotides 271 to 1437 of SEQ ID NO:8, or a functional equivalent thereof, to form a **hybrid** E8-E4 **promoter** capable of regulating expression of a heterologous gene operably linked thereto. The **hybrid promoter** is effective to drive expression of the heterologous gene to a greater degree than the unmodified E4 **promoter**, and preferably at a level of at least about 75-300% of the expression level

obtained by using an unmodified E4 gene **promoter**. The **hybrid promoter** is also ethylene inducible and is capable of directing fruit-specific expression.

DETD A "heterologous" DNA coding sequence is a structural coding sequence that is not native to the **plant** being transformed, or a coding sequence that has been engineered for improved characteristics of its protein product. Heterologous, with respect. . .

DETD A "heterologous" DNA or gene sequence encodes a gene product not normally contiguous or associated with the **promoter** (e.g., an E8-E4 **hybrid promoter** adjacent DNA sequences encoding S-adenosylmethionine cleaving enzyme). In the context of the present invention, a heterologous gene is any DNA. . .

DETD "Constitutive promoter" is any promoter that directs RNA production in many or all tissues of a **plant** transformant at most times.

DETD By "**promoter**" or "**promoter** segment" (e.g., a tomato E8 or E4 **promoter** segment) is meant a sequence of DNA that functions in a **hybrid promoter** disclosed herein to direct transcription of a downstream heterologous gene, and includes **promoter** or **promoter** segments derived by means of ligation with operator regions, random or controlled mutagenesis, addition or duplication of enhancer sequences, addition or modification with synthetic linkers, and the like, having **promoter** activity the functional equivalent of, the E8-E4 **hybrid promoter** described herein or pertinent regions thereof.

DETD By "**plant promoter**" is meant a **promoter** or **promoter** region (as defined above), which in its native form, is derived from **plant** genomic DNA. The **hybrid promoter** of the present invention is a **plant promoter**.

DETD "**Promoter** strength" refers to the level of **promoter** -regulated expression of a heterologous gene in a **plant** tissue or tissues, relative to a suitable standard (e.g., a **hybrid** E8-E4 **promoter** from a particular **plant**, e.g., tomato, versus either the tomato E8 gene or tomato E4 gene **promoter** alone). Expression levels can be measured by linking the **promoter** to a suitable reporter gene such as GUS (.beta.-glucuronidase), dihydrofolate reductase, or nptII (neomycin phosphotransferase II). Expression of the reporter. . .

DETD For the purposes of the present invention, a high level E4/E8 **hybrid promoter** is one that drives expression of a particular gene, such as a reporter gene, at about 75-300% of the levels obtained with either the non-**hybrid** E4 or E8 gene **promoter** derived form the same source.

DETD As used herein, a "**plant** cell" refers to any cell derived from a **plant**, including undifferentiated tissue (e.g., callus) as well as **plant** seeds, pollen, progagules and embryos.

DETD The present invention is directed to the applicants' discovery of a **hybrid promoter** prepared by a combination of regions derived from an E8 and an E4 **promoter** that is capable of directing high level expression of heterologous genes.

DETD To summarize, the present invention is based upon the surprising discovery of a high-level **hybrid** E8-E4 **promoter** which (i) is capable of driving expression of a heterologous gene at significantly greater levels than either the unmodified E8. . . promoters alone, (ii) retains the fruit and ripening-specific function of the parent regulatory regions and (iii) is effective in the **plant** from which the E4 and E8 **promoter** sequences were derived (e.g., tomato), as well as in other plants (e.g., muskmelon, apple and pear).

DETD The parent promoters from which the **hybrid promoter** is derived were selected due to a number of features, and in particular, their ability to regulate expression of the. . .

DETD The SAMase gene encodes the enzyme S-**adenosyl-methionine** hydrolase. The isolation, cloning and sequence of the

SAMase gene is described in U.S. Pat. No. 5,589,623, and in International. . . . as AdoMet hydrolase (AdoMeta[redacted], or by its other name, S-adenosylmethionine cleaving enzyme (SAMase) (Studier, et al.). When expressed in **plant** cells, AdoMetase is effective to "short circuit" a branch of the biosynthetic pathway that produces ethylene, thereby reducing ethylene production. . .

DETD The effects of ethylene on plants, whether produced by the **plant** itself or applied exogenously, are numerous and of considerable commercial importance. Among the diverse physiological effects are leaf abscission, fading. . .

DETD Normally, ethylene production from **plant** tissue is low. Large quantities of ethylene, however, are produced during ripening and senescence processes, and are also produced following. . . tissues, exposure to only a small amount of ethylene may cause an avalanche of ethylene production in adjacent plants or **plant** tissues such as fresh produce. This autocatalytic effect can be very pronounced and lead to loss of fruit quality during. . .

DETD Thus, in one aspect, the present invention provides a method to regulate **plant** cell expression of any gene in a tissue or development stage-specific manner, in particular, genes whose products reduce ethylene synthesis in **plant** cells, using a **hybrid promoter** of the type described herein.

DETD Returning now to the tomato E8 and E4 genes from which segments of the exemplary **hybrid promoter** are derived, the intact parent promoters, the tomato E8 and the tomato E4 **promoter**, are ethylene inducible (Deikman, et al., 1992; Xu, et al., 1996).

DETD . . . E4 and E8 promoters may be used to isolate functionally equivalent promoters from other plants. For example, the raspberry E4 **promoter** may be obtained from a raspberry homologue of the tomato E4 gene. Accordingly, the tomato E4 and E8 promoters can be used to isolate functionally equivalent promoters or partial sequences thereof from additional other types of plants, and those **promoter** sequences used to make **hybrid** E4/E8 promoters.

DETD III. Construction of a **Hybrid** E8-E4 **Promoter**

DETD The E8-E4 **hybrid promoter** contains a combination of nucleotide segments as exemplified by those derived from the tomato E8 and E4 genes. These segments, when combined in a 5'-to-3' fashion, are capable of providing a **promoter** having certain features, as will be described below.

DETD The component polynucleotide segments of the **hybrid promoter** were determined on the basis of experiments conducted in support of the invention, as described in Examples 1-7.

DETD The E8-E4 **hybrid promoter** is composed of a polynucleotide segment derived from an E8 gene **promoter** which is fused to a polynucleotide segment derived from an E4 gene **promoter** positioned downstream of the E8 **promoter** segment. The E8 **promoter**-derived polynucleotide segment preferably includes at least 30 contiguous nucleotides selected from the region extending from nucleotide positions -2257 to -847 of the tomato E8 **promoter** which corresponds to approximately nucleotides 1 to 1411 of SEQ ID NO:7, or the functional equivalent thereof. The E8 **promoter** sequence of SEQ ID NO:7 consists of the E8 **promoter** described by Deikman and Fischer, 1988 and Deikman, et al., 1992, extended on the 5' end, as described in Example 1. The polynucleotide segment derived from a E4 gene **promoter** preferably includes at least 200 contiguous nucleotides selected from the region extending from nucleotide positions -1150 to +16 of the. . .

DETD The construction of exemplary vectors containing the **hybrid promoter** is typically carried out as described in Examples 1-6. The sequence of the tomato E8 **promoter** for use in the present invention is provided in SEQ ID NO:7, and the DNA sequence of regions relevant to. . . FIGS. 2A and 2B (SEQ ID NO:1) and FIG. 10 (SEQ ID

NO:6), respectively. The sequence of the tomato E4 **promoter** has also been publis[redacted] (Cordes, et al., 1989), and t[redacted] DNA sequences corresponding to segments pertinent to the invention are. . .

DETD Polynucleotide segments used to construct the **hybrid promoter** can be obtained by PCR amplification of tomato genomic DNA, using primers designed on the basis of the information presented. . .

DETD The polynucleotide segments which make up the **hybrid promoter** were determined on the basis of expression results for transgenes driven by two representative **hybrid** promoters (FIG. 11), the long E8-E4 **hybrid promoter** (SEQ ID NO:1) and the short E8-E4 **hybrid promoter** (SEQ ID NO:6). Both versions of the **hybrid promoter** were highly effective in driving expression of an exemplary transgene coding for SAMase, as indicated by Western blot results shown in FIGS. 6 and 7, which depict the results of studies on expression of SAMase driven by **hybrid** E4/E8 promoters derived from tomato in musk melon. The **hybrid** promoters were significantly more active in driving expression than either the tomato E8 or tomato E4 **promoter**.

DETD The exemplary long E8/E4 **hybrid promoter** contains an E8 polynucleotide segment corresponding to nucleotides from about -2257 to -1103 of a tomato E8 **promoter**, while the short E8/E4 **hybrid promoter** contains an E8 polynucleotide segment corresponding to nucleotides from about -1529 to -847 of the E8 **promoter**. In expression experiments carried out in support of the invention, the short E8 **promoter** segment was generally found to function as effectively as the long E8 **promoter** segment to enhance overall activity of the **hybrid promoter**. This was surprising in view of previous reports indicating that DNA sequences necessary for both ethylene responsiveness and overall mRNA levels reside in the E8 **promoter** region encompassed by the longer E8/E4 **hybrid promoter** and not the shorter version (Deikman, et al., 1992).

DETD The E8 polynucleotide region encompassed by both versions of the **hybrid promoter** spans positions from about -2257 to -847 of the tomato E8 promter. On the basis of these results, **hybrid** promoters of the invention will contain an E8 **promoter**-derived polynucleotide segment which preferably includes at least 30 contiguous nucleotides selected from this region. In one particular embodiment of the. . .

DETD The suitability of a particular E8 segment for use in constructs employing the **hybrid promoter** can be evaluated in expression experiments employing a heterologous reporter gene. A particular E8 segment selected according to the above guidelines is ligated to a downstream E4 **promoter** segment using the methods described herein. Expression levels of a suitable reporter gene driven by the resulting **hybrid** E8/E4 **promoter** are then compared to expression levels for the same gene regulated by the corresponding E8 or E4 **promoter** alone.

DETD An E8 polynucleotide segment suitable for forming a **hybrid promoter** is one which, when combined with an E4 **promoter** polynucleotide segment corresponding to those described herein and placed in a **hybrid promoter**, drives expression of a reporter gene at a level of at least about 75-300% of the expression level obtained using either an unmodified E4 or E8 gene **promoter** operably linked to said reporter.

DETD Turning now to the E4 polynucleotide segment of the **hybrid promoter**, an examination of the long E8/E4 **hybrid promoter** reveals an E4 polynucleotide segment corresponding essentially to the full-length E4 **promoter**, while the short E8/E4 **hybrid promoter** contains an E4 segment spanning from nucleotide positions -315 to +16 of the E4 **promoter**. As discussed above, both illustrative versions of the **hybrid** E8/E4 **promoter** were effective in directing expression of a heterologous gene (e.g., Examples 5 and 6). The high

activity of the short E8/E4 **hybrid** was surprising, since studies on the E4 **promoter** alone indicate that both upstream and downstream elements are required for ethylene-responsive transcription (Xu, et al., 1996).

DETD The E4 polynucleotide region encompassed by both versions of the **hybrid promoter** spans nucleotide positions from about -1150 to +16 of the tomato E4 promter. On the basis of these results, **hybrid** promoters of the invention will contain an E4 **promoter**-derived polynucleotide segment which preferably includes at least 200 contiguous nucleotides selected from this region. In one particular embodiment of the. . .

DETD . . . E8 component. Moreover, it will be appreciated that the above-described segments refer to functional equivalents thereof, and encompass promoters or **promoter** segments derived by means of ligation with operator regions, random or controlled mutagenesis, addition or duplication of enhancer sequences, addition or modification with synthetic linkers, and the like, having **promoter** activity similar to the E8-E4 **hybrid promoter** described herein or pertinent regions thereof.

DETD IV. Chimeric Genes, Vector Construction and **Plant** Transformation

DETD The E8/E4 **hybrid promoter** of the invention can be used to regulate expression of heterologous genes.

DETD In support of the present invention, two exemplary chimeric genes containing an E8/E4 **hybrid promoter** sequence operably linked to a heterologous DNA sequence, were constructed, long E8/E4:SAMase (pAG-7162) and short E8/E4:SAMase (Examples 1 and 3).. . . predicted to function more efficiently if expressed (i) in high levels and (ii) in a tissue specific manner. Accordingly, the **hybrid promoter** described herein represents an ideal **promoter** to satisfy this objective, and can be used to express any heterologous gene fitting the above-description.

DETD A. **Plant** Transformation Vectors

DETD **Plant** transformation vectors, containing an E8/E4 **hybrid promoter**/transcription-regulatory sequence, are constructed according to methods known in the art (see, for example, Houck and Pear, 1990, and Becker, et. . .

DETD In one embodiment, the chimeric genes of the present invention have two components: (i) a **hybrid** E8/E4 **promoter** and (ii) a heterologous DNA coding sequence.

DETD . . . DNA coding sequences of interest. The transcription of such inserted DNA is then under the control of a suitable E8/E4 **hybrid promoter** (e.g., corresponding to SEQ ID NOs:1, 6).

DETD Further, the vectors of the present invention may include selectable markers for use in **plant** cells (such as the nptII kanamycin resistance gene). The vectors may also include sequences that allow their selection and propagation. . .

DETD The vectors of the present invention may also be modified to intermediate **plant** transformation plasmids that contain a region of homology to an Agrobacterium tumefaciens vector, a T-DNA border region from Agrobacterium tumefaciens, and chimeric genes or expression cassettes. Further, the vectors of the invention may comprise a disarmed **plant** tumor inducing plasmid of Agrobacterium tumefaciens. Other suitable vectors may be constructed using the promoters of the present invention and standard **plant** transformation vectors, which are available both commercially (Clontech, Palo Alto, Calif.) and from academic sources (Waksman Institute, Rutgers, The State. . .

DETD The vectors of the present invention are useful for tissue and/or stage-specific expression of nucleic acid coding sequences in **plant** cells. For example, a selected peptide or polypeptide coding sequence can be inserted in an expression cassette of a vector. . .

DETD Further, the invention includes a method for producing a transgenic fruit-bearing **plant**, wherein fruit produced by the **plant** has a modified phenotype. In this method a chimeric gene is introduced (e.g., by transformation) into progenitor cells of the **plant**. An exemplary chimeric gene is composed of (i) a DNA sequence encoding a gene product effective to modify a phenotypic characteristic of the **plant**, e.g., to reduce ethylene biosynthesis in fruit produced by the **plant**, operably linked to (ii) a promoter whose expression is inducible, e.g., during fruit ripening, by a **plant** cytokine, or by ethylene synthesis by the fruit. As above, the DNA sequence is heterologous to the promoter and the chimeric gene contains the appropriate regulatory elements necessary for expression in a **plant**. Transformed progenitor are grown cells to produce a transgenic **plant** bearing fruit. The method further includes transforming progenitor cells of the **plant** with a selectable vector containing the chimeric gene. The DNA sequences and promoters may be as described above.

DETD . . . vectors, chimeric genes and DNA constructs of the present invention can be sold individually or in kits for use in **plant** cell transformation and the subsequent generation of transgenic plants.

DETD . . . homologue of the tomato E4 or E8 gene. To detect the presence of an E4 or E8 gene in various **plant** species, e.g., strawberry, melon, carnation, cauliflower or raspberry, a southern blot experiment is carried out.

DETD E4 or E8 homologues are identified in a Southern blot of the genomic DNA of a **plant** of interest, probed with a labeled DNA fragment containing the coding sequence of, e.g., the tomato E4 or E8 gene.

DETD . . . (iii) contacting the probe molecules with a plurality of target DNA molecules derived from the genome of a selected fruit-bearing **plant** under conditions favoring specific hybridization between the probe molecule and a target molecule homologous to the probe molecule.

DETD . . . concentration, and are expected to preserve only specific hybridization interactions, allowing the identification and isolation of homologous genes in different **plant** species.

DETD . . . may be isolated from the respective species, by screening a genomic DNA library, e.g., a library derived from a fruit-bearing **plant**.

DETD . . . ability to provide high level tissue and/or stage specific gene expression in transgenic plants, where expression is regulated by a **hybrid** E8/E4 **hybrid promoter**. The E8/E4 **hybrid promoter** of the present invention includes a region or regions of DNA that regulates transcription of the immediately adjacent (downstream) gene to a specific **plant** tissue. According to methods of the present invention, heterologous genes are linked to the promoters of the present invention.

DETD Other genes of interest that could be used in conjunction with the **hybrid** E8/E4 **promoter** include, but are not limited to other ripening modification genes in addition to AdoMetase. Representative examples of such genes include. . .

DETD . . . polygalacturonase inhibiting protein, PGIP, from Phaseolus vulgaris (Toubart, et al., 1992). Also contemplated are the use of modified forms of **plant** glucanase, chitinase and other pathogenesis related (PR) genes (Melchers, et al., 1993, 1994; Ponstein, et al., 1994; Woloshuk, et al.,. . . DNA constructs of the present invention. The expression of these products would be improved when used with a high-level, fruit-specific **promoter** such as the **hybrid promoter** of the present invention.

DETD . . . for example, arabidopsis lycopene cyclase; GENBANK), (iii)

enzymes or other catalytic products such as ribozymes, or catalytic antibodies that modify **plant** cell processes, (iv) ethylene production, such as antisense molecules, enzymes that degrade precursors of ethylene biosynthesis, catalytic products or cosuppression molecules, (v) fungal control, e.g., alternative fungal control genes, (vi) production or levels of **plant** hormones, (vii) the cell cycle or cell division, and (viii) sucrose accumulation, such as the sucrose phosphate synthase gene (GENBANK). . .

DETD A number of methods, in addition to Agrobacterium-based methods, may be employed to elicit transformation of **plant** progenitor cells, such as electroporation, microinjection, and microprojectile bombardment. These methods are well known in the art (Comai and Coning,. . . et al., 1988; Miki, et al. 1987; Bellini, et al., 1989) and provide the means to introduce selected DNA into **plant** genomes. Such DNA may include a DNA cassette which consists of a E8/E4 **hybrid promoter** functionally adjacent to heterologous sequences encoding a desired product, for example, AdoMetase coding sequences.

DETD E. Expression in Heterologous **Plant** Systems

DETD In looking now at experiments carried out in support of the invention, an evaluation of different promoters was conducted. Illustrative **plant** transformation experiments were carried out in muskmelon (Cucumis melo), using SAMase as the exemplary heterologous gene.

DETD . . . using Agrobacterium-mediated transformation and binary vectors containing a series of fruit and ripening-specific promoters from tomato (Table 2). Exemplary synthetic **hybrid** promoters containing different fruit-specific and ethylene-responsive **promoter** domains were prepared (i.e., the long and short E8/E4 **hybrid** promoters) to determine their ability to enhance fruit and ripening specific gene expression.

DETD . . . (-) designation represent negative controls. In looking now at the results presented in FIG. 8, the pAG-7162-derived event (long E8/E4 **hybrid promoter**) is clearly reduced in its ability to produce ethylene during ripening, to an extent significantly greater than that of either of the E4 or E8-**promoter** driven events. Reduced ethylene synthesis and delayed ripening correlated with SAMase gene expression levels determined by Western blotting.

DETD The long E8/E4 **hybrid promoter**-driven events demonstrate reduced ethylene biosynthesis, when compared to both the negative controls and to the other non-**hybrid promoter** -driven events. This is an indication of the greater expression activity of the **hybrid promoter** of the invention when compared to various non-**hybrid** promoters derived from different types of **plant** genes.

DETD As demonstrated herein, the E4/E8 **hybrid promoter** sequences may be isolated from a type of **plant** other than the **plant** to be transformed. This is exemplified by the activity of an E4/E8 **hybrid promoter** composed of tomato-derived sequences which is effective to express a heterologous gene, e.g., the SAMase gene in muskmelon. Alternatively, the E4/E8 **hybrid promoter** sequences may be isolated from the same type of **plant** as that which is transformed by a vector which contains an E4/E8 **hybrid promoter** and a heterologous coding sequence, e.g. the SAMase gene. For example, a raspberry E4/E8 **hybrid promoter** may be operably linked to a heterologous gene, such as the SAMase gene, and used to transform raspberries.

DETD Long E8/E4 **Hybrid Promoter** (2.8 kb) and Preparation of Intermediate Vector pAG-1762

DETD To obtain a portion of the tomato E8 **promoter** for use in preparing a **hybrid promoter**, a plasmid containing

the 2.0 kb tomato E8 **promoter**, pAG-1742, was digested with XbaI and BamHI using standard molecular biology protocols (Sambrook, et al., 1989). The sequence of the. . .

DETD . . . used as a source of the HindIII fragment that is the approximately -2257 to -1103 bp upstream region of the **hybrid** E8/E4 **promoter** of the present invention, corresponding to nucleotides 1-1155 of SEQ ID NO:7. This fragment was inserted 5' of the approximately 1122 bp E8 **promoter** in pAG-5321 at the HindIII and XbaI sites (FIG. 4).

DETD To isolate a full-length E4 **promoter** for use in constructing a **hybrid promoter**, a 10.6 kb fragment containing the tomato E4 **promoter** was excised from a second plasmid, pAG-1752, by treatment with XbaI and BamHI. The sequence of the tomato E4 **promoter** has been published (Cordes, et al., 1989), and the DNA sequence of the minus 1150 to plus 16 base pair. . .

DETD Preparation of Binary Vector, pAG-7162 Containing Long E8/E4 **Hybrid Promoter**

DETD Preparation of a Short E8/E4 **Hybrid Promoter** and an Intermediate Transfer Vector, pAG-126

DETD . . . intermediate vector combining truncated polynucleotide segments derived from the tomato E4 and E8 gene promoters to form a short E8/E4 **hybrid promoter** fused to the coding sequence for SAMase, was prepared as follows.

DETD The resulting short E8.backslash.E4 **promoter** fragment was then purified and ligated into a suitable plasmid vector. The vector, which contained the SAMase gene, was digested with HindIII and NcoI in order to orient the **hybrid promoter** immediately upstream of the SAMase gene, with both the **promoter** and gene positioned in the same 5' to 3' direction.

DETD The resulting intermediate plasmid containing a short E8.backslash.E **hybrid promoter**::SAMase construct was designated pAG-126 and is presented in FIG. 4.

DETD Preparation of a Binary Vector Containing a Short E8/E4 **Hybrid Promoter**

DETD Plasmid pAG-126 was digested with HindIII and KpnI to produce a 1.5 kb fragment containing the E8/E4 **hybrid promoter** coupled to the SAMase gene. The excised fragment was gel purified.

DETD The 1.5 kb short E8/E4 **hybrid promoter**::SAMase fragment was then ligated to the binary vector to produce plasmid, pAG-7182, as shown in FIG. 5.

DETD In looking now at the results presented in FIG. 8, the pAG-7162-derived event (long E8/E4 **hybrid promoter**) is clearly reduced in its ability to produce ethylene during ripening, to an extent significantly greater than that of either of the E4 or E8-**promoter** driven events. The long E8/E4 **hybrid promoter**-driven events demonstrate reduced ethylene biosynthesis, when compared to both the negative controls and to the other non-**hybrid promoter**-driven events.

DETD . . . FEATURE:
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<222> LOCATION: (1)...(2327)
<223> OTHER INFORMATION: n = A,T,C or G
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<223> OTHER INFORMATION: n = A,T,C or G

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<223> OTHER INFORMATION: n = A,T,C or. . .

CLM What is claimed is:

1. A chimeric gene comprising a tomato E4/E8 **hybrid** **promoter** comprising, in the 5' to 3' direction: a first nucleotide segment consisting of nucleotides 1 to 1156 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment consisting of nucleotides 271 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8.

2. A chimeric gene comprising a tomato E4/E8 **hybrid** **promoter** comprising, in the 5' to 3 direction: a first nucleotide segment comprising nucleotides 729 to 1411 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment comprising nucleotides 1107 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8.

3. A chimeric gene comprising a tomato E4/E8 **hybrid** **promoter** comprising, in the 5' to 3' direction: a first nucleotide segment consisting of nucleotides 729 to 1411 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment consisting of nucleotides 1107 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8.

. . . chimeric gene according to claim 1, 2, or 3, further comprising a heterologous DNA coding sequence operably linked to said **hybrid** **promoter**.

5. The chimeric gene according to claim 4, wherein said **hybrid** **promoter** drives fruit-specific expression of the heterologous DNA coding sequence in a **plant**.

8. A **plant** cell comprising the chimeric gene according to any one of claims 1, 2, or 3.

9. A method of producing a transgenic fruit-bearing **plant** characterized by reduced ethylene production during fruit ripening, comprising the steps of: (i) introducing into progenitor cells of said **plant**, a DNA construct comprising: a **hybrid** E4/E8 **promoter** sequence comprising in the 5' to 3' direction a first nucleotide segment comprising nucleotides 729 to 1411 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment comprising nucleotides 1107 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8; and a heterologous DNA sequence which encodes a a protein which reduces ethylene biosynthesis operably linked to the E4/E8 **promoter**, to produce transformed progenitor **plant** cells; and (ii) regenerating the transgenic fruit-bearing **plant** from the transformed progenitor cells, wherein fruit of the transgenic fruit-bearing **plant** have reduced ethylene production during fruit ripening relative to fruit of a non-transformed **plant**.

. . . The method according to claim 9, wherein expression of the heterologous DNA sequence in the fruit of said transgenic fruit-bearing **plant** results in delayed ripening of the fruit relative to fruit from a non-transformed **plant**.

12. The method according to claim 10, wherein the **plant** is a Cucumis sp.

13. The method according to claim 10, wherein said E4/E8 **hybrid promoter** comprises a first nucleotide segment consisting of nucleotides 1 to 1156 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment consisting of nucleotides 271 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8.

14. The method according to claim 10, wherein said E4/E8 **hybrid promoter** comprises a first nucleotide segment consisting of nucleotides 729 to 1411 of the tomato E8 gene **promoter** sequence presented as SEQ ID NO:7 fused to a second nucleotide segment consisting of nucleotides 1107 to 1437 of the tomato E4 gene **promoter** sequence presented as SEQ ID NO:8.

L7 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:763350 CAPLUS
DOCUMENT NUMBER: 126:101772
TITLE: Tissue-specific expression conferred by the S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar
AUTHOR(S): Mijnsbrugge, Kristine Vander; Van Montagu, Marc; Inze, Dirk; Boerjan, Wout
CORPORATE SOURCE: Lab. Genetica, Dep. Genetics, Flanders Interuniv. Inst. Biotechnol., Univ. Gent, Ghent, B-9000, Belg.
SOURCE: Plant Cell Physiol. (1996), 37(8), 1108-1115
CODEN: PCPHA5; ISSN: 0032-0781
PUBLISHER: Japanese Society of Plant Physiologists
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Tissue-specific expression conferred by the S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar
AB In Arabidopsis the promoter of the gene encoding S-**adenosyl**-L-**methionine** synthetase (SAM-S) Psam-1 confers expression preferentially in the vascular tissue. In search for promoters that drive expression in particular cells of the lignifying tissues in trees, we have analyzed the expression pattern conferred by the Psam-1 promoter in transgenic poplar. Histochem. analyses demonstrated .beta.-glucuronidase (GUS) activity mainly in phloem and cortex tissue throughout the **plant**, and in root tips. Fluorimetric assays showed high GUS activity in the tissues outside (phloem, cortex and cork) compared to those inside (xylem and pith) of the cambial layer. In contrast, the endogenous SAM-S activity was high in tissues inside and low in tissues outside of the cambial layer. RNA gel blot anal. demonstrated a high transcript level of the endogenous sam-s gene(s) in tissues both outside and inside the cambial layer. This indicates that the low SAM-S activity in the bark was at least partially due to translational and/or pos-translational regulation of the endogenous sam-s gene(s). In dormant transgenics, the tissue specificity was conserved, but the activity levels were up to 10-fold reduced.
IT Cambium

(Arabidopsis Psam-1 promoter functional in vascular tissue outside of; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Promoter (genetic element)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Psam-1; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT **Plant** tissue
(cortex, promoter functional in; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Gene expression
(from Psam-1 promoter, post-transcriptional regulation in poplar of; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Poplar (Populus tremula)
(**hybrid** with Populus alba; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase **promoter** of Arabidopsis thaliana in transgenic poplar)

IT Poplar (Populus alba)
(**hybrid** with Populus tremula; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase **promoter** of Arabidopsis thaliana in transgenic poplar)

IT Cork
Phloem
(promoter functional in; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Dormancy (**plant**)
(promoter tissue-specificity and; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Genes (**plant**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sam-1, promoter of; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT Arabidopsis thaliana
Poplar
(tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT **Plant** tissue
(vascular, promoter preferentially functional in; tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

IT 9012-52-6, S-**Adenosyl**-L-**methionine** synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tissue-specific expression conferred by S-**adenosyl**-L-**methionine** synthetase promoter of Arabidopsis thaliana in transgenic poplar)

=> d history

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L2 2364 S L1 AND PLANT

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L5            2 DUP REM L4 (0 DUPLICATES REMOVED)
L6           22 S L2 AND (ADENOSYL AND METHIONINE)
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=> s promoter and plastocyanin and (s()adenosyl()methionine)

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=> d l9 ibib abs


L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1999:405103  CAPLUS
DOCUMENT NUMBER:          131:54757
TITLE:                    Chimeric promoters derived from Arabidopsis and
                          Agrobacterium for constitutive expression in plants
INVENTOR(S):              Stuiver, Maarten Hendrik; Sijbolts, Floor Hendrik
PATENT ASSIGNEE(S):       Mogen International N.V., Neth.
SOURCE:                   PCT Int. Appl., 44 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 9931258         A1   19990624       WO 1998-EP8162   19981210
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             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     ZA 9811228         A    19990614       ZA 1998-11228    19981208
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     EP 1038013         A1   20000927       EP 1998-964512   19981210
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 9813502         A    20001010       BR 1998-13502    19981210
PRIORITY APPLN. INFO.:                     EP 1997-203912   A  19971212
                                           WO 1998-EP8162   W  19981210
AB   The invention describes promoters comprising a minimal promoter
     and transcription-activating elements which mediate constitutive
     transcription in most parts of a plant.  Examples include a set of
     promoters where one is more active in the green parts of a plant and
     another in the underground parts, specifically a promoter
     derived from the ferredoxin promoter of Arabidopsis thaliana and
     the rolD promoter from Agrobacterium rhizogenes, and a
     promoter derived from the S-adenosyl-
     methionine synthetase and plastocyanin promoters of
     Arabidopsis.
REFERENCE COUNT:          8
REFERENCE(S):             (1) Benfey, P; US 5097025 A 1992 CAPLUS
                          (2) Cambridge Advanced Tech; WO 9720056 A 1997 CAPLUS
                          (3) Chua, N; WO 9412015 A 1994 CAPLUS
                          (4) Comai, L; US 5106739 A 1992 CAPLUS
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(5[redacted]Cui Decai; WO 9514098 A 1995 CA[redacted]US
AL[redacted]CITATIONS AVAILABLE IN THE RE F[redacted]MAT

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=> d history

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     15:18:51 ON 02 JAN 2002
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L3             0 S L2 AND (FERRODOXIN OR FERRODOXINE) AND ROLD
L4             2 S L2 AND (PLASTOCYANIN)
L5             2 DUP REM L4 (0 DUPLICATES REMOVED)
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=> s promoter and ferredoxin and rold

L10            1 PROMOTER AND FERREDOXIN AND ROLD

=> s l10 not l9

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